

Modeling of in hospital mortality determinants in myocardial infarction patients, with and without stroke: A national study in Iran

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Background: The data and determinants of mortality due to stroke in myocardial infarction (MI) patients are unknown. This study was conducted to evaluate the differences in risk factors for hospital mortality among MI patients with and without stroke history. **Materials and Methods:** This study was a retrospective, cohort study; 20,750 new patients with MI from April, 2012 to March, 2013 were followed up and their data were analyzed according to having or not having the stroke history. Stroke and MI were defined based on the World Health Organization's definition. The data were analyzed by logistic regression in STATA software. **Results:** Of the 20,750 studied patients, 4293 had stroke history. The prevalence of stroke in the studied population was derived 20.96% (confidence interval [CI] 95%: 20.13–21.24). Of the patients, 2537 (59.1%) had ST-elevation MI (STEMI). Mortality ratio in patients with and without stroke was obtained 18.8% and 10.3%, respectively. The prevalence of risk factors in MI patients with and without a stroke is various. The adjusted odds ratio of mortality in patients with stroke history was derived 7.02 (95% CI: 5.42–9) for chest pain resistant to treatment, 2.39 (95% CI: 1.97–2.9) for STEMI, 3.02 (95% CI: 2.5–3.64) for lack of thrombolytic therapy, 2.2 (95% CI: 1.66–2.91) for heart failure, and 2.17 (95% CI: 1.6–2.9) for ventricular tachycardia. **Conclusion:** With regards to the factors associated with mortality in this study, it is particularly necessary to control the mortality in MI patients with stroke history. More emphasis should be placed on the MI patients with the previous stroke over those without in the interventions developed for prevention and treatment, and for the prevention of avoidable mortalities.

Key words: Mortality, myocardial infarction, risk factor, stroke

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INTRODUCTION

Stroke, after myocardial infarction (MI), is the second leading reason for mortality in Iran as with many countries worldwide.^[1-3] The epidemiology of stroke has already been investigated in the American, European, African, and Asian countries.^[4-11] No comprehensive study has yet investigated the epidemiology of stroke, particularly in MI patients, in Iran, one of the largest countries in Southwest Asia. Stroke and MI share many risk factors, most prevalent of which are smoking,

dyslipidemia, type 2 diabetes, and hypertension.^[12-14] Coronary heart disease is highly preventable in stroke patients.^[15]

The risk factors for stroke and MI, especially smoking, hypertension, and dyslipidemia are highly prevalent in Iran, as well.^[16-18] According to projections, stroke continues to be the second leading cause of mortality worldwide till 2030.^[19] Urbanism, increased life expectancy, reduction in childbirth, aging and elderly population, epidemiological changes, socioeconomic status, geographical conditions, and lifestyles such as poor diet, stress, and low mobility are the main causes

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of the burden of noncommunicable diseases, particularly stroke.^[20,21]

Because the determinants of stroke in different communities are various,^[5,21,22] we require knowledge about the risk factors and determinants of mortality in a community for effective planning and selection of appropriate strategies for the prevention and management of stroke and heart attack as the most important causes of death.^[23,24]

Since no comprehensive study has yet been investigated the status and mortality determinants of stroke in MI patients in Iran, this study is conducted to determine and compare the determinants of mortality due to stroke in MI patients.

MATERIALS AND METHODS

In this retrospective cohort study, the data obtained from the MI Registry of Iran's Cardiovascular Diseases Surveillance System were analyzed. Around 20,750 hospitalized patients with MI with a new presentation (hospitalized in 540 hospitals) between April, 2012 and March, 2013 were enrolled. All the patients' data were entered into a computerized retrospective observational data bank. The study was approved by the Management Center of Noncommunicable Diseases and the Department of Cardiovascular Diseases Prevention of Iran's Ministry of Health and Medical Education (approval no. 305/837). The research followed the principles of the Declaration of Helsinki; the researchers did not conduct any interventions on the patients, and an Institutional Review Board approved this research. The study protocol was approved by an Independent Scientific Review Committee (at Shahid Beheshti University Medical of Sciences) (no. 1392-1-85-12129). Inclusion criteria were determined according to the World Health Organization (WHO) and World Heart Federation definition of MI diagnosis per the International Classification of Diseases-10 codes I21 and I22.^[1]

Patients with MI history or no definite diagnosis by a cardiologist were excluded from the study. The data on age, gender, education, ischemic heart disease symptoms, hospital stay duration, smoking, dyslipidemia, hypertension, type 2 diabetes, heart failure, and family history of cardiovascular diseases were gathered. Stroke history was defined based on the WHO's definition "rapidly developing signs of focal (or global) disturbance of cerebral function lasting >24 h (unless interrupted by surgery or death), with no apparent nonvascular cause." Therefore, patients with transient cerebral ischemia or stroke events were excluded if they had blood disease or brain tumors. Moreover, patients with secondary strokes caused by trauma, acute hemorrhagic stroke, or transient ischemic attack were excluded.^[10,25] After a definite diagnosis of MI

by a cardiologist, the data on the left bundle branch block, right bundle branch block, atrial fibrillation, ventricular and atrial tachycardia, type and site of MI, and use of therapeutic regimens such as coronary artery bypass grafting, percutaneous coronary intervention, and thrombolytic therapy were recorded.

Statistical analysis

The cohort of patients was defined by the date at MI diagnosis, hospital stay, and follow-up till discharge or death (outcome). Hospital mortality due to MI was considered a dependent variable. Odds ratio (OR) of mortality for clinical and demographic risk factors were calculated by logistic regression. OR of mortality was calculated as the crude and adjusted ratio for patients with and without stroke by simple and multiple logistic regression models. First, univariate analysis was conducted. To control confounders, we entered the significant or approximately significant variables into a multiple regression model. For data analysis, Chi-square, *t*-test, and regression model in Stata software (Stata Corp. 2011, Stata Statistical Software: Release 14, College Station, TX: Stata Corp LP, USA) were used and $P < 0.05$ was considered the level of significance.

RESULTS

Of the 20,750 studied patients with MI, 4293 had a stroke history. The prevalence of stroke in the studied population was derived 20.96% (confidence interval CI 95%: 20.13–21.24). Mean standard deviation age at MI incidence was 64.38 (12.9) years in patients with stroke history and 60.37 (13.3) years in patients without, with a significant difference ($P < 0.001$). Half of the patients with stroke history had 30–64-year-old. About 43.6% of them had 65–84-year-old and 5.4% 85–106. About 64.8% of these patients were male, 52.8% of them were illiterate, and only 4.9% had an academic education. The prevalence of smoking was derived 23.9% in them. The prevalence of diabetes, hypertension, hypercholesterolemia, and heart failure was obtained 30%, 56.5%, 27.3%, and 8.1% in patients with stroke history and 20.1%, 30%, 15.4%, and 8% in patients without stroke history, respectively. The ratio of cardiovascular surgery, percutaneous coronary intervention, and thrombolytic therapy was obtained 6.4%, 5.8%, and 41.1% in the former group and 1.6%, 7.1%, and 45.3% in the latter, respectively. The demographic characteristics and individual risk factors in patients with and without stroke are shown in Table 1.

Within 1 year of study, 18.8% of the stroke patients deceased. The mortality ratio in all patients was derived 12.1%. Of the 4293 patients with stroke, 2537 (59.1%) had ST-elevation MI (STEMI). Mortality ratio was obtained 18.8% in patients

Table 1: Demographic and medical history of myocardial infarction patients with and without stroke

| Characteristic | Total (%) | With stroke | Without stroke | P |
|--|---------------|--------------|----------------|--------|
| Sample size | 20,750 | 4293 (20.69) | 16,457 (79.31) | - |
| Age (mean±SD) (years) | 61.2±13.4 | 64.38±12.9 | 60.37±13.9 | 0.001* |
| Hospital stay (days) | 6.5±14.6 | 6.5±14.3 | 6.5±14.6 | 0.805 |
| Gender | | | | |
| Men | 15,033 (72.4) | 2784 (64.8) | 12,249 (74.5) | 0.001* |
| Women | 5717 (27.6) | 1509 (35.2) | 4208 (25.5) | |
| Education | | | | |
| Illiteracy | 9611 (46.3) | 2269 (52.8) | 7342 (44.6) | 0.001* |
| Primary | 4941 (23.8) | 963 (22.4) | 3978 (24.1) | |
| Guidance | 1940 (9.3) | 339 (7.9) | 1601 (9.7) | |
| High school | 2992 (14.4) | 511 (11.9) | 2481 (15) | |
| University | 1266 (6.1) | 211 (4.9) | 1055 (6.4) | |
| Smoker | 5443 (26.2) | 1302 (30.3) | 4141 (25.16) | 0.001* |
| Diabetes | 4612 (22.2) | 1290 (30) | 3322 (20.1) | 0.001* |
| Hypertension | 7376 (35.5) | 2425 (56.5) | 4951 (30) | 0.001* |
| High cholesterol | 3710 (17.8) | 1174 (27.3) | 2536 (15.4) | 0.001* |
| Heart failure | 1682 (8.1) | 351 (8.1) | 1331 (8) | 0.850 |
| Family history of cardiovascular disease | 7179 (34.6) | 1446 (33.6) | 5733 (34.8) | 0.157 |

*P<0.05 considered significant. SD=Standard deviation

stroke history and 10.3% in the without. The clinical characteristics and risk factors in the patients according to the type of hospital diagnosis and therapeutic measures are shown in Table 2. The ratio of cardiovascular surgery, percutaneous coronary intervention, and thrombolytic therapy was obtained, respectively, 6.4%, 5.8%, and 41.1%. By logistic regression, the mortality-associated factors were different in the MI patients with and without stroke history. The OR of the studied factors is shown in Table 3. The adjusted OR of mortality in patients with stroke history was derived 7.02 (95% CI: 5.42–9) for chest pain resistant to treatment, 2.39 (95% CI: 1.97–2.9) for STEMI, 3.02 (95% CI: 2.5–3.64) for lack of thrombolytic therapy, 2.2 (95% CI: 1.66–2.91) for heart failure, and 2.17 (95% CI: 1.6–2.9) for ventricular tachycardia. Considering other potential covariates and the confounders of hospital mortality in patients with stroke, we obtained the highest adjusted OR of hospital mortality in patients with stroke for chest pain resistant to treatment followed by lack of thrombolytic therapy and STEMI.

DISCUSSION

In this study, the risk factors in the MI patients with and without stroke history were investigated and compared for the first time in Iran. In reliable, electronic databases such as PubMed and Scopus, we found no study to model and compare the characteristics of the two groups of patients as with our study. Our study indicated that the pattern of determinants of hospital MI mortality with and without a stroke is various. The mean age at incidence in our study is similar to a study in Singapore comparing the risk factors for stroke in Chinese, Indian, and Malaysian ethnic

populations. The study in Singapore reported the mean age of stroke patients to be 64.1 years. In the study of Singapore, hypertension and hypercholesterolemia were found to be the most prevalent risk factors. The prevalence of hypertension was obtained 83.2%, 85%, and 84.1% in Chinese, Malaysian, and Indian ethnics, respectively, which is twice higher than the prevalence of hypertension in the patients in Iran.^[10,11] Moreover, the prevalence of smoking was obtained 11.8%, 20%, and 15.9% in Chinese, Malaysian, and Indian ethnics in Singapore, respectively. The prevalence of smoking was obtained approximately 24% in our study, which is higher than that reported by the study of Singapore. In the study of Singapore, the prevalence of diabetes was reported to be 67.5% in Malaysian ethnics and 39.8% in Chinese ethnics while it was 27.9% in the patients of our study. Within 1 year of study, hospital mortality was obtained 9.1%, 3.4%, and 2.5% in Indian, Chinese, and Malaysian ethnics, respectively. The corresponding figure was obtained 32% in the patients of our study. This inconsistency can be explained by the difference in lifestyles, life expectancy, and the incidence of stroke risk factors. Another explanation can be related to access to therapeutic and hospital services to prevent mortality due to stroke. However, it is noteworthy that the sample size in the study of Singapore seems unsatisfactorily small, which might be another reason for the inconsistency of the findings.^[11]

A review article reported that the age at stroke incidence was 68.6 years in men and 72.9 years in women, and the incidence and prevalence of stroke were higher in men than women. Although the age of incidence in our study is younger than the age reported in this review article, the gender differences in our study and this review article

Table 2: Prevalence of clinical risk factors in myocardial infarction patients with and without stroke

| Characteristic | Total (%) | With stroke | Without stroke | P |
|------------------------------|---------------|-------------|----------------|-------|
| AF | 511 (2.5) | 203 (4.7) | 485 (2.9) | 0.001 |
| VT | 1198 (5.8) | 277 (6.4) | 921 (5.6) | 0.032 |
| RBBB | 289 (1.4) | 81 (1.8) | 208 (1.2) | 0.002 |
| LBBB | 383 (1.8) | 160 (3.7) | 223 (1.3) | 0.001 |
| Lateral MI | 990 (4.8) | 228 (5.3) | 762 (4.6) | 0.062 |
| Anterior MI | 4332 (20.9) | 789 (18.3) | 3543 (21.5) | 0.001 |
| Inferior MI | 7179 (34.6) | 1446 (33.6) | 5733 (34.8) | 0.157 |
| Posterior MI | 853 (4.2) | 143 (3.3) | 710 (4.3) | 0.004 |
| STEMI | 15,729 (75.8) | 2537 (59.1) | 10,568 (64.2) | 0.001 |
| Death | 2511 (12.1) | 808 (18.8) | 1703 (10.3) | 0.001 |
| PCI | 1431 (6.9) | 252 (5.8) | 1179 (7.1) | 0.003 |
| CABG | 539 (2.6) | 275 (6.4) | 264 (1.6) | 0.001 |
| Lack of thrombolytic therapy | 9222 (44.5) | 1767 (41.1) | 7455 (45.3) | 0.001 |
| Chest pain | 2229 (10.7) | 401 (9.3) | 1828 (11.1) | 0.001 |

AF=Atrial fibrillation; VT=Ventricular tachycardia; RBBB=Right bundle branch block; LBBB=Left bundle branch block; MI=Myocardial infarction; STEMI=ST-segment elevation myocardial infarction; NSTEMI=Non-ST-segment elevation myocardial infarction; PCI=Percutaneous coronary intervention; CABG=Coronary artery bypass grafting

Table 3: Risk factors for hospital mortality in myocardial infarction patients with and without stroke

| Characteristics | With Stroke | | | Without Stroke | | |
|------------------------------|-------------|-----------|-------|----------------|-----------|-------|
| | OR | CI | P | OR | CI | P |
| Standardized age (year) | 1.52 | 1.36-1.69 | 0.001 | 1.47 | 1.38-1.58 | 0.001 |
| Women | 1.26 | 1.03-1.53 | 0.019 | 1.21 | 1.06-1.38 | 0.003 |
| Education | | | | | | |
| Illiterate | 0.82 | 0.53-1.27 | 0.385 | 0.84 | 0.65-1.08 | 0.180 |
| Primary | 0.70 | 0.45-1.10 | 0.125 | 0.76 | 0.59-0.98 | 0.037 |
| Guidance | 0.39 | 0.22-0.69 | 0.001 | 0.750 | 0.55-1 | 0.053 |
| High school | 0.62 | 0.38-1.02 | 0.061 | 0.71 | 0.54-0.93 | 0.016 |
| University | Reference | 1 | - | 1 | 1 | - |
| Smoking | 0.90 | 0.74-1.09 | 0.291 | 1.33 | 1.17-1.50 | 0.001 |
| Diabetes | 1.06 | 0.86-1.30 | 0.551 | 1.10 | 0.96-1.27 | 0.159 |
| Hypertension | 0.60 | 0.50-0.72 | 0.001 | 0.95 | 0.83-1.08 | 0.461 |
| High cholesterol | 0.77 | 0.63-0.95 | 0.016 | 0.91 | 0.78-1.07 | 0.301 |
| Chest pain | 7.02 | 5.42-9 | 0.001 | 3.72 | 3.27-4.25 | 0.001 |
| Lack of thrombolytic therapy | 3.02 | 2.5-3.64 | 0.001 | 2.98 | 2.64-3.36 | 0.001 |
| RBBB | 0.54 | 0.26-1.09 | 0.09 | 3.24 | 2.26-4.63 | 0.001 |
| VT | 2.17 | 1.6-2.90 | 0.001 | 1.98 | 1.61-2.43 | 0.001 |
| STEMI | 2.39 | 1.97-2.90 | 0.001 | 4.29 | 3.80-4.86 | 0.001 |
| PCI | 0.88 | 0.57-1.35 | 0.565 | 0.57 | 0.42-0.78 | 0.001 |
| CABG | 0.68 | 0.45-1.02 | 0.063 | 1.35 | 0.91-1.99 | 0.126 |
| Heart failure | 2.2 | 1.66-2.91 | 0.001 | 1.38 | 1.15-1.65 | 0.001 |

OR=Odds ratio; CI=Confidence interval; RBBB=Right bundle branch block; VT=Ventricular tachycardia; STEMI=ST-segment elevation myocardial infarction; PCI=Percutaneous coronary intervention; CABG=Coronary artery bypass grafting

are consistent.^[26,27] The prevalence of stroke in our study was 20.96% higher than Japanese patients. A nationwide multicenter cooperative cohort study of Japanese patients with MI and stroke reported stroke history (14.7%) to be

more frequent than MI history (2.6%) in patients with stroke, whereas stroke history (6.6%) was less frequent than MI history (7.6%) in patients with MI.^[28] The mean age at MI incidence in our study is lower than a study in Australia that reported the mean age of patients with stroke was 78.6 years. The difference in lifestyle, life expectancy, and patterns of risk factors for noncommunicable diseases as well as the larger elderly population of Australia can be some reasons for the discrepancy in the mean age at the incidence of stroke. In a study in Nigeria, the prevalence of hypertension and dyslipidemia was reported to be 69.4% and 21.1%, respectively. The difference in the population and environment of the study may be the main reasons for the inconsistency of the findings.^[5] In a study in Australia and Europe (Finland, Norway, Belgium, France, Germany, the Netherlands, Switzerland, Italy, Greece, and Hungary), 3944 patients with stroke were studied, and smoking, dyslipidemia, and hypertension were reported to be the most prevalent (48.7%, 45.8%, and 35.9%, respectively) risk factors for stroke, which are, except hypertension, higher than our study. The prevalence of diabetes and heart failure in the study in Europe was obtained 6.5–11.1% and 3.8–4.2%, respectively,^[12] which is lower than the corresponding figures in our study. The study in Europe has recommended that adoption of a primary strategy to avoid a stroke in young adolescents and the intervention aimed to change and/or decrease the highly prevalent risk factors that can be mitigated is an important principle of the stroke control. In Brazil, the risk factors for stroke were studied, and the prevalence of hypertension, diabetes, and stroke history was reported to be 29.9%, 9.1%, and 2.1%, respectively, which are lower than the present study.^[29] In a study in Japan, 1389 incidence of stroke were registered from 1988 to 2004. The mean age at incidence was 73.3 years in men and 76.8 years in women. Moreover, the prevalence of hypertension, diabetes, dyslipidemia, smoking, and heart attack was 55%, 19.3%, 17.9%, 25.9%, and 6.9%, respectively.^[30] In another study in Japan, the fatality rate due to stroke was obtained 14.9% and 15.7% in men and women, respectively. Since life expectancy is much higher in Japan than Iran and the mean age at stroke incidence is expected to be younger in Iran than Japan, the determinants of hospital mortality in our study are similar to a study reporting that MI history, diabetes, gender, and age are the most common determinants of outcome in intracerebral hemorrhage patients.^[30] Interestingly, the prevalence of risk factors in the MI patients without stroke in Iran and Japan is similar. The prevalence of manageable risk factors is being controlled in patients with stroke and MI and was obtained lower compared to other studies. In a review article, the fatality rate of stroke within a month after the onset of the disease was reported to be 17% in Japan, 33% in Italy, and 22.9% overall. The fatality of stroke has been derived 32.1%, which is higher than Italy. The difference may be explained by the access to better therapeutic services in hospitals and health-care facilities

in Italy compared with Iran. In a study in Iran, losing the golden time to start thrombolytic therapy, lack of beds in the Intensive Care Units, and failure to afford the facilities and services were some of the obstacles to initiating the treatment in stroke and MI patients.^[14] In Iran, MI patients with stroke history appear to control and mitigate the risk factors themselves.^[18,24] Our study is the first report in Iran and indicated that the pattern of determinants of hospital MI mortality with and without a stroke is various. Therefore, adopting an appropriate strategy for the treatment and prevention of death in the two groups of the patients requires close attention to the characteristics of each group of the patients. In addition, our study demonstrated that the risk factors including hypertension, diabetes, smoking, dyslipidemia, and heart failure were more prevalent in MI patients with stroke history than those without. MI patients without stroke history appear to control and mitigate the risk factors themselves. Therefore, it is recommended to give greater priority to the MI patients with the previous stroke over those without in Iran for training, healthcare, and control of the risk factors such as hypertension, diabetes, and smoking to enhance the cost-effectiveness of the interventions for prevention and treatment and to prevent avoidable mortalities. As no similar study was found to make a closer comparison between our and others' findings, similar studies in other countries are needed to confirm the present study findings.

Limitations of the study

In this study only the MI patients who died in hospital were investigated. Hence, the findings can be generalized only to hospitalized patients. In addition, tissue plasminogen activator thrombolytic therapy was not considered in MI patients with the previous stroke. We did not gather any treatment information about these patients before MI. Because no similar study, to the best of our knowledge, was found to compare our and others' findings more closely, similar studies in other countries should be conducted to give more definite explanations.

CONCLUSION

We used a large-scale database in Iran. Our study demonstrated that the risk factors including hypertension, diabetes, smoking, dyslipidemia, and heart failure were more prevalent in the MI patients with a stroke history than those without. In fact, the MI patients without stroke history appear to control and mitigate the risk factors themselves. Chest pain resistant to treatment gave the highest adjusted OR of hospital mortality in patients with stroke followed by no thrombolytic therapy and STEMI. It is recommended to give greater priority to the MI patients with the previous stroke over those without in Iran for training, healthcare, and control of the risk factors as well as to enhance the

cost-effectiveness of the interventions for prevention and treatment.

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Conflicts of interest

The authors have no conflicts of interest.

AUTHORS' CONTRIBUTORS

AA, AK and KE contributed to the design of the research protocol and supervised its implementation. AA and KE analysed the data and AA, AK and KE drafted the article. All of the authors approved the final version of the manuscript before publishing and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All of the authors reviewed drafts of the article and contributed to the conceptual framework.

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